

REMARKS

Reconsideration of the above-identified application in view of the amendment above and the remarks below is respectfully requested.

Claims 57-63 have been canceled in this paper. Claims 41-43 have been amended in this paper. No new claims have been added in this paper. Therefore, claims 1-11 and 34-55 are pending and are under active consideration.

Claims 1-11, 42-48 and 57-63 stand rejected under 35 U.S.C. 103(a) "as being unpatentable over Putter et al (US Pat No 3,699,158 dt. Oct. 17th 1972)." In support of the rejection, the Patent Office states the following:

The instant claims are directed to various deuterated catecholamine derivatives of the general **formula I**, *currently amended*. Further, pharmaceutical compositions containing deuterated catecholamine derivatives are embodied in the instant application.

Determination of Scope and content of the Prior Art (MPEP § 2141.01)

Putter et al teach selective deuterated compounds/intermediates specifically selective deuterated tyrosine (see column 2, lines 30-50).

Ascertainment of the difference between the Prior Art and Claims (MPEP §2141.02)

The difference between the instant compounds and Putter et al is that the instant compounds require a di deuterated hydroxyl attached to the aromatic ring and whereas in the prior art the tyrosine has mono deuterated hydroxy.

Finding of prima facie obviousness – rational and motivation (MPEP § 142-2143)

Accordingly, one of ordinary skill in the art would be motivated to prepare the instant compounds by modifying the process of deuteration depending on the substrate as taught by Putter and a skilled artisan would modify the prior art process by introducing the DOPA or analogues of DOPA and subject them to selective deuteration and an ordinary artisan is expected to have reasonable success in synthesizing the instant product/compositions.

The examiner contends that the above reference is proper and an ordinary artisan would have had a reasonable expectation of success at the time of the instant invention to arrive at the instant compounds/compositions and hence it is *prima facie* [obvious.] (Emphasis in original.)

Insofar as the subject rejection relates to claims 57-63, the rejection is moot in view of Applicant's cancellation of claims 57-63 in this paper. Insofar as the subject rejection relates to claims 1-11 and 42-48, Applicant respectfully traverses the subject rejection.

As best understood by Applicant, the Patent Office appears to be contending that it would have been obvious to make the compound of claim 1 because Putter et al. teaches a deuterated tyrosine that differs from the claimed compound in that the Putter compound includes a single hydroxyl substituent on its aromatic ring member whereas the claimed compound includes two hydroxyl substituents on its aromatic ring member. Applicant respectfully disagrees that a person of ordinary skill in the art would have been motivated to modify the Putter compound to include a second hydroxyl group. This is because the mono-hydroxyl compound of Putter et al. is tyrosine whereas the di-hydroxyl compound of claim 1 is a catecholamine compound, such as L-DOPA. The utilities of tyrosine and L-DOPA are well-known to be vastly different from one another, tyrosine functioning as an amino acid and L-DOPA functioning as a precursor for dopamine. MPEP 2144.09 provides that a rejection based on close structural similarity is proper only when the compounds in question have similar utilities. Therefore, in view of the known dissimilar utilities of tyrosine and L-

DOPA, one of ordinary skill in the art would not have been motivated to make a modification to L-DOPA based merely on the teaching in Putter et al. of a modification to tyrosine.

Moreover, claims 42-48 are further patentable over Putter et al. for at least the reason that Putter et al. does not teach or suggest combining the compound of claim 1 or its physiologically compatible salts with pharmaceutically compatible adjuvants and additives to form a pharmaceutical composition. In fact, there is absolutely no teaching or suggestion anywhere in Putter et al. to use the Putter compounds to make pharmaceuticals. Instead, the only uses disclosed in Putter et al. for the Putter compounds are as intermediates in the preparation and study of labeled peptides, polypeptides and proteins and as a growth medium for biological investigations (see Putter et al. at Abstract and at col. 1, lines 22-30). None of these uses would have suggested combining the Putter compounds or their physiologically compatible salts with pharmaceutically compatible adjuvants and additives.

Accordingly, for at least the above reasons, the subject rejection should be withdrawn.

Claims 1, 34-41 and 49-55 stand rejected under 35 U.S.C. 112, first paragraph, “as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.” In support of the rejection, the Patent Office states the following:

Claims 1, 34-41 and 49-55 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the synthesis of the deuterated catecholamine derivatives, does not reasonably provide enablement for a method of treatment of dopamine deficiency diseases or the enlisted diseases in the instant claims.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Enablement is considered in view of the *Wands factors* (MPEP 2164.01(a)) as the instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors.

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability of unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the existence of working examples; (8) the quantity of experimentation necessary. All of the *Wands factors* have been considered with regard to the instant application, with the most relevant factors discussed below.

Nature of the Invention

All of the rejected claims are drawn to an invention which pertains to a method for the treatment of dopamine deficiency diseases or diseases which are based on disrupted tyrosine transport and as enlisted in the instant claims and further the method comprising administering to a patient in need thereof an effective amount of the deuterated catecholamine derivative according to claim 1 as well as physiologically compatible salt.

Breadth of the Claims

The complex nature of the claims is greatly exacerbated by breadth of the claims. Claims 1, 34-41 and 49-55 encompass a method of treatment of acute psychoses and a method for the production of pharmaceuticals for the prophylaxis of psychoses is rather unclear.

Guidance of the Specification/Working Examples

There is no guidance given by the specification as to what type of administration is rendered to the patient in need.

All of the guidance provided by the specification is directed towards synthesis of deuterated catecholamines in the instant application. (See examples 1-7 pages 19-24 of the specification).

Predicability of the Art

The instant application is directed to a method of dopamine deficiency diseases, for the treatment of amyotrophic lateral sclerosis. Further, in the treatment of inhibiting prolactin secretion, and a method for the production of pharmaceuticals for the prophylaxis of psychoses as well as for the treatment of acute psychoses is rather broad and unclear.

In the instant case, the instant methods are highly unpredictable since one skilled in the art cannot fully describe, visualize or recognize the identity of the invention and unable to predict which compound is used in the treatment of which disease.

The amount of Experimentation Necessary

In order to practice claimed invention of one skilled in the art would have to first envision a combination of appropriate compound or composition and an appropriate model system and test the combination in the model system to determine whether or not the combination is effective or not. If successful, which is unlikely given the lack of significant guidance from the specification, one skilled in the art would have to then either envision a modification of the combination or envision an entirely new combination of the above, and test the desired compound again, whose success is unpredictable. Therefore, it would require undue experimentation to practice the claimed invention to develop deuterated catecholamines as claimed in the instant application.

Hence, the method of treatment as embodied in the instant claims in the absence of the above factors has not been considered as enabled by the instant specification. (Emphasis in original.)

Applicant respectfully traverses the subject rejection. As best understood by Applicant, the Patent Office appears to be taking the position that the rejected claims lack enablement due to an

alleged lack of operability for the asserted utilities. For at least the reasons below, Applicant respectfully submits that the Patent Office is in error.

With respect to claim 1, Applicant notes that claim 1 is directed at a class of deuterated catecholamine derivatives. There is no recitation in claim 1 of any particular utility for the claimed class of deuterated catecholamine derivatives. As a result, the compounds of claim 1 meet the enablement requirement **unless** the Patent Office can prove that a person of ordinary skill in the art, after having read the present specification, would have had a reasonable basis for doubting that the compounds of claim 1 have **any** utility. Applicant respectfully submits that the Patent Office has failed to meet its burden of proof in casting a reasonable doubt about any such utility. The present specification teaches that L-DOPA is well-known for having utility in the treatment of Parkinson's disease and restless leg syndrome. Based on a comparison of the chemical structures of L-DOPA and, for example, the deuterated analogues of L-DOPA of claim 1, there would have been no reason for a person of ordinary skill in the art to doubt that the deuterated analogues of L-DOPA of claim 1 have utility in the treatment of Parkinson's disease and restless leg syndrome. Similarly, without any contrary evidence tending to cast doubt on the utility of the remaining compounds of claim 1, one of ordinary skill in the art would have believed these remaining compounds also to have utility in the treatment of Parkinson's disease and restless leg syndrome.

With respect to claim 41, Applicant has herein amended the claim so that it no longer specifies a particular utility. As a result, claim 41 is enabled for at least the same reasons discussed above in connection with claim 1.

With respect to claims 34-40 and 49-55, Applicant notes that these claims do recite particular utilities. However, the Patent Office has failed to prove why a person of ordinary skill in the art at

the time of filing the application, after having read the specification, would have had a reasonable basis for doubting the recited utilities. MPEP 2164.04 makes clear that it is the burden of the Patent Office to prove a lack of enablement and **not** the Applicant's burden to prove enablement. This means that, where, as in the present case, Applicant discloses a particular utility, the Patent Office must accept that disclosed utility unless the Patent Office can prove that a person of ordinary skill in the art would have had a reasonable basis for doubting the disclosed utility. Applicant respectfully submits that the Patent Office has failed to meet its burden in the present case. The Patent Office has provided no documentary or other evidentiary support for its position that the claims lack enablement. Instead, all that the Patent Office has done is to provide a series of unsubstantiated statements and conclusions using the framework of the *Wands* analysis. However, Applicant notes that the Patent Office's *Wands* analysis is completely devoid of any documentary or other evidentiary support. For example, there is no documentary or other evidentiary support for the Patent Office's statement, on page 7, lines 3-5, that “[i]n the instant case, the instant methods are highly unpredictable since one skilled in the art cannot fully describe, visualize or recognize the identity of the invention and unable to predict which compound is used in the treatment of which disease.” Similarly, there is no documentary or other evidentiary support for the Patent Office's statement on page 7, lines 10-14, that “[i]f successful, which is unlikely given the lack of significant guidance from the specification, one skilled in the art would have to then either envision a modification of the combination or envision an entirely new combination of the above, and test the desired compound again, whose success is unpredictable.” In short, it is clear from the above that the Patent Office has taken the position that the specification is non-enabling unless Applicant can prove otherwise. Such a position constitutes clear error.

Accordingly, for at least the above reasons, the subject rejection should be withdrawn.

In conclusion, it is respectfully submitted that the present application is now in condition for allowance. Prompt and favorable action is earnestly solicited.

If there are any fees due in connection with the filing of this paper that are not accounted for, the Examiner is authorized to charge the fees to our Deposit Account No. 11-1755. If a fee is

required for an extension of time under 37 C.F.R. 1.136 that is not accounted for already, such an extension of time is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on December 17, 2007

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